Can Non-Invasive Sampling Determine the Inflammatory Status of the Intra-uterine Environment?

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Can Non-invasive Sampling Determine the Inflammatory Status of the Intra-uterine Environment?

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OBJECTIVE: To determine the differential expression of inflammatory mediators in various maternal-fetal compartments and identify the best non-invasive sampling that can predict the intra-uterine environment.

STUDY DESIGN: Term, non-laboring patients without major maternal or fetal complications undergoing cesarean delivery were asked to provide samples during the immediate pre-operative and intra-operative period: maternal plasma via venipuncture, 2-3ml of unstimulated saliva, urine via foley catheter, and cervical and vaginal secretions via directed speculum examination. Amniotic fluid was obtained intra-operatively via needle aspiration of the intact amniotic sac after hysterotomy. These fluids were analyzed for 27 inflammatory mediators using the Bio-Plex array. We compared the inflammatory mediator profile between all compartments as well as mediator levels from non-invasive samples (maternal blood, urine, saliva, vaginal and cervical secretions) with invasive sampling (amniotic fluid). Correlation among mediators in the various compartments was determined using Spearman correlation with P <0.05 required for significance.

RESULTS: Twenty patients were included in this study. Among the non-invasive compartments studied, none of the inflammatory mediators were significantly correlated with amniotic fluid. When comparing cervical secretions to vaginal (posterior fornix) secretions, 25 of the 27 mediators reached a significant correlation, with correlation co-efficients ranging from 0.460 to 0.943. None of the remaining non-invasive compartments were significantly correlated with each other.

CONCLUSION: In term, non-laboring patients, there does not appear to be correlation of inflammatory mediators between amniotic fluid and non-invasive maternal-fetal compartments. It remains to be determined if this finding is the same in preterm pregnancies or in the presence of labor. There is no difference in the inflammatory mediator profile between cervical and posterior fornix vaginal secretions.

Background and Objective:

- Previous studies have shown that the amniotic fluid cytokine profile is predictive of pregnancy outcome in patients at risk for preterm delivery.
- Currently, determination of the intra-amniotic inflammatory melieu requires invasive testing with its associated risks.
- Perhaps a better understanding of the causes of preterm labor and effects of treatment can be achieved if the inflammatory status could be determined in a non-invasive manner.

Objectives:

- To determine the differential expression of inflammatory mediators in various maternal-fetal compartments.
- To identify the best non-invasive sampling that can predict the intra-uterine environment.

Methods:

- Term, non-laboring patients without major maternal or fetal complications undergoing cesarean delivery were asked to provide samples during the immediate pre-operative and intra-operative period
- The timing, location, and collection method of each sample is shown in Table 1.
- Samples were analyzed for 27 mediators including cytokines, chemokines, and growth factors via the Bio-Plex™ Suspension Array system.
- We compared the inflammatory mediator profile between all compartments as well as mediator levels from non-invasive samples (maternal blood, urine, saliva, vaginal and cervical secretions) with invasive sampling (amniotic fluid).
- Correlation among mediators in the various compartments was determined using Spearman correlation with P <0.05 required for significance.

Results:

- Twenty patients were included in this study.
- Table 2 displays the cytokines which reached a significant correlation between compartments.
- Among the non-invasive compartments studied, none of the inflammatory mediators were significantly correlated with amniotic fluid.
- When comparing cervical secretions to vaginal (posterior fornix) secretions, 25 of the 27 mediators reached a significant correlation, with correlation co-efficients ranging from 0.460 to 0.943.
- None of the remaining non-invasive compartments were significantly correlated with each other.

Conclusions:

- In term, non-laboring patients, there does not appear to be correlation of inflammatory mediators between amniotic fluid and non-invasive maternal-fetal compartments.
- It remains to be determined if this finding is the same in preterm pregnancies or in the presence of labor.
- There is no difference in the inflammatory mediator profile between cervical and posterior fornix vaginal secretions.

Table 1. Timing, Location, and Collection Method of Samples

Compartment	Collection Method
Collected at Time of Consent	
Maternal serum	Venipuncture
Maternal saliva	Unstimulated salivation into collection container
Collection in Operating Room after Regional Anesthesia	
Maternal urine	Test tube from foley catheter
Cervical secretions	Weck-Cell Sponge via speculum-directed exam
Vaginal fluid	Weck-Cell Sponge via speculum-directed exam
Collected During Cesarean Delivery	
Amniotic fluid	Via catheter/needle after hysterotomy prior to rupture of membranes
Collected Post-operatively	
Placenta	After examination, 2x2 cm portion taken and transported in culture media to lab for in vitro culture

Table 2. Correlation among Cytokines in Maternal-Fetal Compartments (P <0.05)

Compartment	Amniotic Fluid	Maternal Serum	Urine	Cervical Secretions	Vaginal Secretions	Saliva	Placental Culture
Amniotic Fluid		1				1	2
Maternal Serum	MIP1b		2	3	4	5	
Urine		IL13, PDGF		1			6
Cervical Secretions		IP10, TNFα, VEGF	MCP1		25	4	3
Vaginal Secretions		GCSF, IP10, PDGF, TNFα		GCSF, Eotaxin, GMCSF, IFNγ, IL-1b,1ra,2,4,5,6,7,8,9,10,12, 13,15,17,IP10,MCP1,MIP1b,		2	4
Saliva	IL7	Eotaxin IL13, IL15, MIP1a, TNFα		IFNγ, IL4, IL5, IL17	IL17, FGF		2
Placental Culture	IL5, RANTES		IL1ra, IL-2, 4, 10, 13, VEGF	MIP1b, RANTES, VEGF	IL2, IL8, MCP1, MIP1b	IP10, RANTES	

KEY:
- The number of mediators with significant correlations between the compartments is in the upper-right half of table.
- The names of the mediators which were significantly correlated are in the bottom-left half of the table.
- Color coding has been used to aid in matching corresponding boxes.
- Interleukin (IL), platelet derived growth factor (PDGF), fibroblast growth factor (FGF), granulocyte colony stimulating factor (G-CSF), granulocyte macrophage stimulating factor (GM-CSF), interferon gamma (IFN-γ), inducible protein-10 (IP-10), monocyte chemotactic protein-1 (MCP-1), macrophage inflammatory protein (MIP), tumor necrosis factor alpha (TNF-α), vascular endothelial growth factor (VEGF), regulated on activation normal T cell expressed and secreted (RANTES)